| TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371 | | Attorney's Docket Number 08059.0001 U.S. Application No. 09/529128 |
|---|---|---|
| International Application. No. PCT/NZ98/00147 | International Filing Date 6 October 1998 | Priority Date Claimed 10 October 1997 |

**Title of Invention: DRUG DELIVERY SYSTEM**

**Applicants For DO/EO/US: Graham Francois DUIRS**

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.
3. [ ] This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. [X] A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [X] is transmitted herewith (required only if not transmitted by the International Bureau).
   b. [ ] has been transmitted by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).
6. [ ] A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. [X] Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)).
   a. [X] are transmitted herewith (required only if not transmitted by the International Bureau).
   b. [ ] have been transmitted by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [ ] have not been made and will not be made.
8. [ ] A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. [ ] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. [X] The annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

**Items 11. to 16. below concern other document(s) or information included:**

11. [ ] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. [ ] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [ ] A FIRST preliminary amendment.
    [ ] A SECOND or SUBSEQUENT preliminary amendment.
14. [ ] A substitute specification.
15. [ ] A change of power of attorney and/or address letter.

16. [ ] Other items or information:
    a. [ ] Verified Small Entity Statement.
    b. [ ] Copy of Notification of Missing Requirements.

| U.S. APPLICATION NO. | INTERNATIONAL APPLICATION NO. | ATTORNEY DOCKET NUMBER |
|---|---|---|
| 09/529128 | PCT/NZ98/00147 | 08059.0001 |

| | CALCULATIONS |
|---|---|
| 17. [X] The following fees are submitted: | |
| **Basic National Fee (37 CFR 1.492(a)(1)-(5)):** | |
| Search Report has been prepared by the EPO or JPO.....$840.00 | |
| International preliminary examination fee paid to USPTO (37 CFR 1.482).....$670.00 | |
| No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2)).....$690.00 | |
| Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO.....$970.00 | $ 970.00 |
| International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4).....$ 96.00 | |
| **ENTER APPROPRIATE BASIC FEE AMOUNT =** | **$ 970.00** |
| Surcharge of $130.00 for furnishing the oath or declaration later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(e)). | $ |

| Claims | Number Filed | Number Extra | Rate | |
|---|---|---|---|---|
| Total Claims | 18-20= | 0 | X $18.00 | $ |
| Independent Claims | 3- 3= | 0 | X $78.00 | $ |
| Multiple dependent claim(s) (if applicable) | | | +$260.00 | $ 260.00 |
| | | **TOTAL OF ABOVE CALCULATIONS =** | | **$ 1230.00** |
| Reduction by 1/2 for filing by small entity, if applicable. Verified Small Entity statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28) | | | | $ |
| | | **SUBTOTAL =** | | **$ 1230.00** |
| Processing fee of $130.00 for furnishing the English translation later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(f)). | | | + | $ |
| | | **TOTAL NATIONAL FEE =** | | **$ 1230.00** |
| Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). | | $40.00 per property | + | $ |
| | | **TOTAL FEES ENCLOSED =** | | **$ 1230.00** |
| | | Amount to be refunded | | $ |
| | | charged | | $ |

a. [X] A check in the amount of **$ 1230.00** to cover the above fees is enclosed.

b. [ ] Please charge my Deposit Account No. _____ in the amount of $_____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. [X] The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 06-0916. A duplicate copy of this sheet is enclosed.

The Commissioner is hereby authorized to charge any other fees due under 37 C.F.R. §1.16 or §1.17 during the pendency of this application to our Deposit Account No. 06-0916.

**SEND ALL CORRESPONDENCE TO:**
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Submitted: April 7, 2000

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# DRUG DELIVERY SYSTEM

## TECHNICAL FIELD

This invention relates to a substance delivery system.

Reference throughout the specification shall be made to the use of the present invention as a drug delivery system for use in animal body cavities, such as the vagina.

Should be appreciated however that the present invention can be used to deliver substances other than drugs and can be used in relation to humans and in other body cavities, for example the rumen, ears, mouth and so forth.

Drug delivery systems are used extensively in controlled breeding and reproductive management. Although considerable research has been invested in the design of these devices, there are still problems associated with them.

Firstly, these devices are required to be retained within the body cavity for the slow release of drugs over a period of time. To facilitate this, various arms and projections have been built into the device which can either engage with the walls of the body cavity, or make the device wide enough such that when in the body cavity the device cannot naturally exit the animal through the entrance orifice.

Major problems with the provision of such arms or projections is that they can irritate or even rupture the lining of the body cavity, causing distress to the animal and providing a site for possible infection. Yet another problem with these projections is that in order for the device to be inserted into the animal, the device will need to be considerably smaller than it is when the projections are fully extended. Thus, the device needs to be designed so the projections

can be retracted or folded away during insertion and removal of the device.

A major problem with drug delivery devices is that traditionally they have been manufactured with the drug impregnated into the material from which the device is made. Typically, this material is in many instances a matrix of silicone.

To manufacture devices from drug impregnated silicone is expensive.

A further disadvantage of using a drug impregnated device is that it is very difficult to dispose. For example, the hormones used in reproductive management are required to be disposed in accordance with heavily regulated environmental procedures. As it is always possible that the drug within the silicone matrix had not been fully delivered to the animal when the device is removed, the whole device will have to be disposed as the whole device is the drug delivery system.

It would be desirable if the devices could be reused.

Another problem with the devices is that they have a specific dose rate which cannot be readily changed. Further with these devices, the treatment cannot be changed or customised according to requirements. For instance, animals at the heavier end of the species weight range may require a dose supplement or a type of breed may vary in size and require a dose change.

It would be desirable if there could be provided a drug delivery device for use inside body cavities which was easy to insert, readily retained within the cavity without irritation to the cavity walls, was reusable, could allow for differing treatments and was comparatively inexpensive.

## BACKGROUND ART

It is an object of the present invention to address the foregoing problems or at least to provide the public with a useful choice.

Further aspects and advantages of the present invention will become apparent from the ensuing description which is given by way of example only.

## DISCLOSURE OF INVENTION

According to one aspect of the present invention there is provided a substance delivery device

characterised in that

the device includes a support frame capable of receiving and releasing a substance delivery means which is capable of releasing substance into a body cavity.

According to another aspect of the present invention there is provided a pod for use with the support frame as described above.

The substance delivery device should now be referred to as a drug delivery device such as an intravaginal release device.

It should be appreciated however that a device in accordance with the present invention can be adapted for use in other body cavities, such as the rumen, the auditory system and so forth. It should also be appreciated that the present invention can be used in both humans and animals.

Further, it should be appreciated that the substance being delivered can be in a variety of forms e.g. liquid, solid bullets, powder, gel and so forth.

The support frame may come in a number of configurations. The main purpose of the support frame is to hold the substance delivery pods in such a manner that they can deliver the substance effectively to the body cavity.

Other requirements of the support frame is that it is naturally retained within the body cavity when required for the delivery of substance, but can also be readily inserted and removed.

The applicant has designed support frames with a number of configurations which meet the above criteria. One particular set of designs the applicant has arrived at has at least one arm which is pliable in movement situations, that maintains a tension across the length of the arm.

According to an alternate aspect of the present invention there is provided a support frame for a drug delivery device having at least one curved arm which can support a substance delivery means.

In some embodiments of the substance delivery means described immediately above may not be removable pods but fixed to the support frame.

However, reference throughout this specification will now be made to the drug delivery device as having removable substance delivery means in the form of pods.

It should be appreciated the prior art devices were fairly inflexible having straight arms rigidly fixed to the main body of this device when *in situ*. In contrast, the applicant has found that a curved arm or arms give considerable pliability and/or tension.

For ease of reference, throughout the specification the support frames shall be referred to as having two arms.

It should be appreciated however that the present invention can have any number of arms and that two arms is merely just one form of a preferred embodiment.

The applicant believes that having arms which are pliable in movement situations means that the device is less harsh on the interface with the mucosal membrane in the vagina. For example, animal movement or change of position will enable the device to flex accordingly to facilitate animal comfort and yet maintain retention integrity characteristics.

One way by which such a design can be achieved is to create a "wishbone" shape. That is, a comparatively short joining piece or base and two arms which curve firstly outwards from the base and then inwards to provide a substantially S-shaped arms.

If the arms curve away from the base so as to form the outline of the bowl, there is no tension where the arms connect to the base. However, there is tension throughout the arms provided by the double curve of the S-shape.

The lack of tension at the base means that the arms can still move with respect to the base if required. However the tension along the length of the arms can cause the arms to bias outwards from the body of the support frame causing the arms or the substance delivery pods attached to arms to extend outwards toward the mucosal membrane, and in some cases exposing the surface of the pods to the mucosal membrane.

It should be noted to here that the mucosal membrane is very effective at transferring drugs to the body. And, while it is not a necessity, it can be beneficial to drug delivery.

It should be appreciated that other configurations are envisaged. For example, one embodiment present invention may be in the shape of a part circle, such as a "bicycle clip" configuration which requires no base: but still has the tension and pliability in the arms. Other embodiments may have the arms, not curving away from the base in a bowl shape, but curving in the opposite direction.

One embodiment may be a single curved arm with one or more pods attached to it.

It should be appreciated that the base can be used to locate and remove the device.

There is now greater choice in the material from which the support frame can be made. This is because present invention obviates the need to impregnate the support frame with the substance to be delivered. This is because in preferred embodiments the drug delivery pods are attachable and removable from the support frame. Thus, manufacture of the support frame is quite independent of the drug delivery system.

In further embodiments however the support frame is made of a plastics material such as nylon which is readily moulded, flexible and is physiologically friendly and reusable. Other materials may of course be used.

The term pod should not be seen as limiting as is intended to mean any article which can be attached to or detached from the support frame and capable of releasing substances such as drugs.

In one embodiment of the present invention the pods may consist only of the drug itself moulded into a shape that can interact with the support frame.

However, preferred embodiments of the present invention the pods are devices

which house or incorporatethe substance to be delivered.

The pods may release the substances into the body cavity by a variety of means. In one embodiment, this may be through a simple process of osmosis of the drug passing through a membrane on the pod.

In other embodiments it may be a device in the pod which applies pressure to the drug pushing it out of the pod for instance, through micropores.

In other embodiments there may be electronically controlled release of the substance.

The pods can take any suitable shape. However, it is preferable that the pods do not have projections which could irritate the lining of the body cavity. Instead, it is envisaged that the outer surfaces of the pods are smooth and possibly rounded. In one embodiment, the pods are substantially egg shaped.

Pods may be made from any suitable material. In one embodiment, the pods may comprise a cellulose matrix which allows the leaching of drugs contained within the matrix into the fluids of the body cavity.

The pods maybe attached to the support frame by a variety of means.

For example, there may be a complementary plug and socket between the pod and the support frame allowing the pod to be readily attached to and subsequently detached from the frame. This would enable reloading of the device to prolong a treatment. The design would also enable concurrent treatments of different drugs or substances to be applied from two or more pods through different stages of a treatment cycle by removing the device and placing new pods for immediate reinsertion thereby creating no disruption to the current treatment cycle and similarly the same treatment may be prolonged

by replacing pods.

Thus, the present invention can provide two or more co-current treatments, two or more sequential treatments or prolong a single treatment. All of which are achievable by the ability to replace pods.

In another embodiment the pod will be configured so as to have a portion of the pod slide into a groove on the support frame (or vice versa).

Other attachment mechanisms may be the mating of uneven surfaces (such as in Velcro™).

Another method may the use of a suitable adhesive.

However, in preferred embodiments the pod is flexibly attached to the support frame allowing full movement of the pod with respect to the support frame. This enables the surfaces of the pod to move gently against the lining of the body cavity (or not at all) even if there is a violent movement of the support frame holding the pods.

It should be appreciated that if the pods have a curved surface as previously described, and the arms are tensioned gently outwards, the flexible attachment allows the surface of the pod to gently contact the mucosal membrane of the vagina without irritation allowing ready transfer of the drugs contained within the pods. It should be noted that some treatments will be enhanced by mucosal membrane contact whereas other treatments can be transmitted effectively through delivery into the vaginal mucosa and fluids.

It is envisaged that there are many ways by which the flexible attachment may be achieved.

In one embodiment this is by a ball and socket arrangement allowing three dimensional movement of the pod with respect to the support frame.

It should be seen that the tensioning of the arms outwards enables the device to be retained in the body cavity when *in situ*. However, the use of pliable arms means that the arms can be moved to allow the device to be effectively compressed to allow ready insertion and withdrawal of the device through the orifice to the body cavity.

In one embodiment, the device is capable of having its arms wrapped around itself or merely compressed together.

In another embodiment to the present invention the arms are capable of interlocking for removal or insertion.

For example, the main body of the arms may be designed such that the stem is made in two adjacent webs that are joined by connecting braces at regular intervals. The adjacent arms of the device facing one another may be slightly offset. This enables the arms to be forced together so the upper arch of wishbones on adjacent webs intertwine to enable the adjacent pods to close together to the narrowest position.

If webs are used, then the device has less material giving a lighter frame and therefore is less likely to cause adverse tissue reactions.

It should be appreciated that the pods can be positioned anywhere in relative to the support frame. However, preferred embodiments of pods are attached at or near the distal end of the arms of the support frame. In some embodiments there may be more than one pod on an arm.

In preferred embodiments of the present invention there is provided a locator

to enable the device *in situ* to be readily located and removed from the animal. This locator in some instances may be an aperture.

It can be seen that the present invention has considerable advantages over the prior art.

Usage of attachable pods enable the support frame of the device to be readily reused which leads to economical savings.

Further, only the pods need to be disposed of giving environmental advantages. Furthermore, the pods can be assessed for residual drug containment and if necessary be disposed according to environmental safety requirements if treatment has not depleted the drug.

The ability to remove pods means that treatment of the animal or human can be changed in the treatment through the removal of the device and the substitution of a pod or more.

Treatments can also be customised with different pods use, perhaps containing different drugs or different dosage rates.

The flexible attachment of the pods to the support frame means that the pods are free moving and able to orientate themselves in accordance with mucosal membrane movement and device orientation. This enables the pods to provide interface with the mucosal membrane in some instances enhance the delivery and transmission of drugs and nutrients.

The wishbone configuration of preferred embodiments provides a gentle tensioning of the arms in comparison with rigid devices used previously.

Manufacture of the support frame is considerably easier than previously as there is no need to consider the impregnation of drugs into material from which the support frame is manufactured.

Finally, the present invention allows for ready insertion and removal.

Aspects of the present invention will now be described by way of example only with reference to the accompanying drawings in which:

Figure 1 diagrammatic view of substance delivery device in accordance with one embodiment on the present invention, and

Figure 2 diagrammatic drawing of the device in figure 1 in an insertion/removal configuration.

With respect to the figures, there is illustrated a drug system delivery device generally indicated by arrow 1.

The device 1 includes a support frame 2 attached to which are substance delivery pods 3.

The support frame 2 is in the form of a wishbone having two arms 4 and 5 substantially S-shaped connected to an elongated base 6.

The base 6 contains a locator, in the form of an aperture 8, for easy location and removal of the device. Note the base is not associated with any flexing which only occurs along the S-shaped arms.

The arms 4 and 5 are curved in such a manner that when *in situ* (refer Figure 1) the distal ends of the arms 7 are biased outwards.

It is envisaged that the configuration of the arms and the flexibility of the material from which the support frame will be made will enable the arms to move in such a fashion so as to cross-over as illustrated in Figure 2. There may be provided webbing (not shown) to interlock the arms. This cross-over configuration allows for ready insertion and removal of the device.

The pods 3 are housings which contain a drug delivered into the body cavity. In this embodiment, housing of pods 3 is cellulose or an appropriate matrix.

The pods 3 are attached to the arms 4 and 5 by a flexible attachment in the form of a ball and socket (not clearly shown).

It can be seen that the curved outer shape of the pods 3 in combination with the biasing of the arms 4 and 5 and the flexible attachment allows free movement of the pods against the mucosal membrane without irritating the membrane.

Aspects of the present invention are described by way of example only and it should be appreciated that modifications and additions may be made thereto without departing from the scope of the appended claims.

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422 Rec'd PCT/PTO 07 APR 2000
PCT/NZ98/00147
Received 05 January 2000

CLAIMS:

1. A substance delivery device for insertion into a body, said device includes a support frame having at least two resilient arms which retain said device in the body cavity, wherein each resilient arm is capable of receiving and releasing a substance delivery means capable of releasing substance into the said body cavity.

2. A substance delivery device as claimed in claim 1, wherein the said substance is a drug.

3. A substance delivery device as claimed in either 1 or claim 2 wherein the said device is an intra-vaginal release device.

4. A substance delivery device as claimed in claim 3 wherein the substance is released from the substance delivery means through osmosis.

5. A substance delivery device as claimed in any one of claims 1 to 4 wherein the substance delivery means are rounded.

6. A substance delivery device as claimed in any one of claims 1 to 5 wherein the substance delivery means is flexibly attached to the arm.

7. A substance delivery device as claimed in claim 6 wherein the substance

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delivery means is attached to the arm by a ball and socket mechanism.

8. A substance delivery means for attachment to a substance delivery device as claimed in any one of claims 1-7.

9. A substance delivery device as claimed in any one of claims 1 to 7 wherein the support frame is in the form of a wish bone.

10. A substance delivery device as claimed in claim 9 wherein the arms are biased outward from a central section of the support frame.

11. A substance delivery device as claimed in either claim 9 or claims 10 characterised in that the support frame is made of nylon.

12. A substance delivery device as claimed in any one of claims 9 to 11 to characterised in that the arms are sufficiently pliable to be moved together to allow the substance delivery device to be effectively compressed.

13. A substance delivery device as claimed in any one of claims 9 to 12 wherein the arms are capable of interlocking for removal or insertion.

14. A substance delivery device as claimed in any one of claims 9 to 13 characterised in that the support frame includes a locator to enable the substance delivery device to be readily located and removed from *in situ*.

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15. A substance delivery device as herein described with reference to and as illustrated by the accompanying drawings.

16. A substance delivery means substantially as herein described with reference to and as illustrated by the accompanying drawings.

**FIG 1**

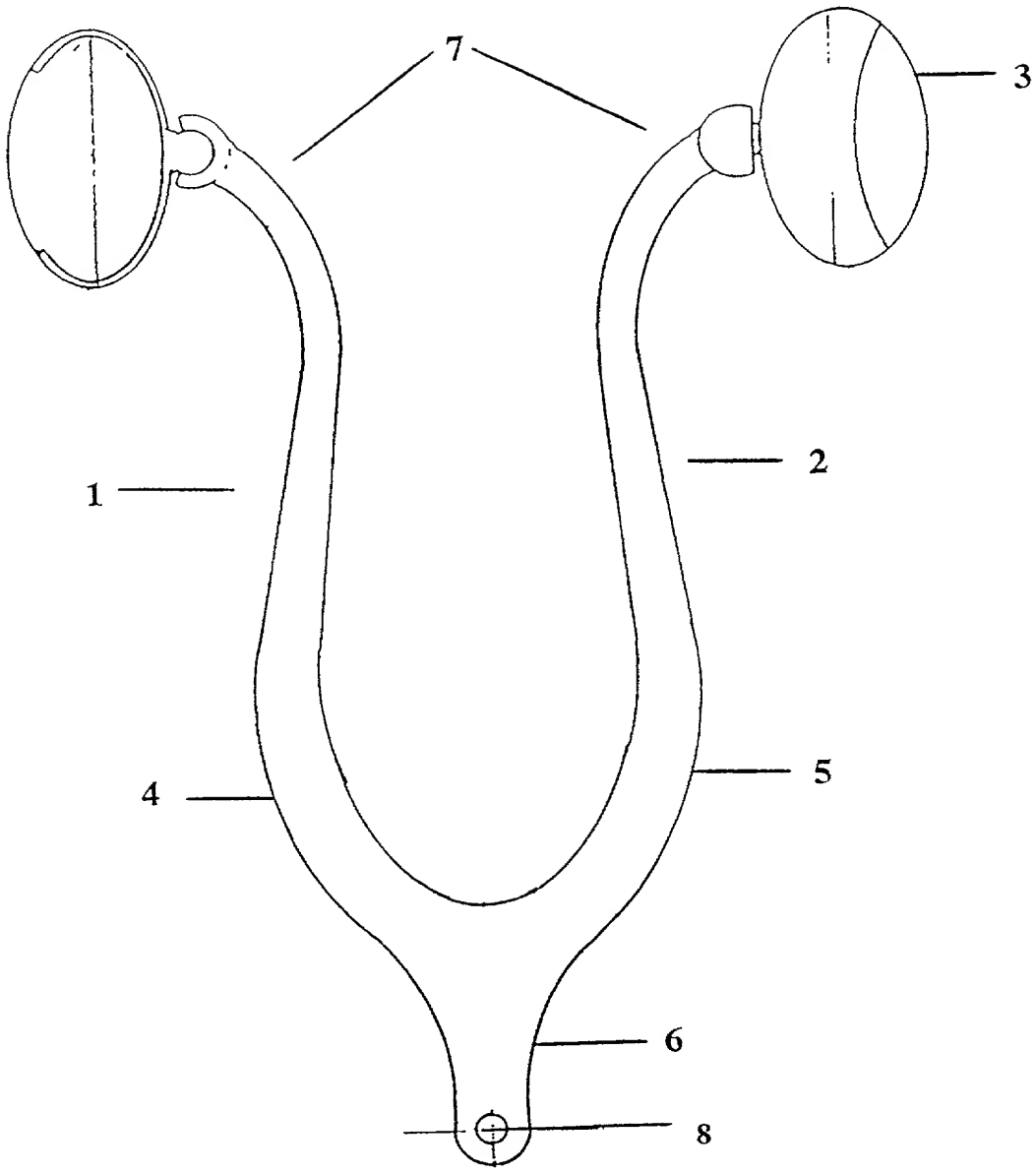
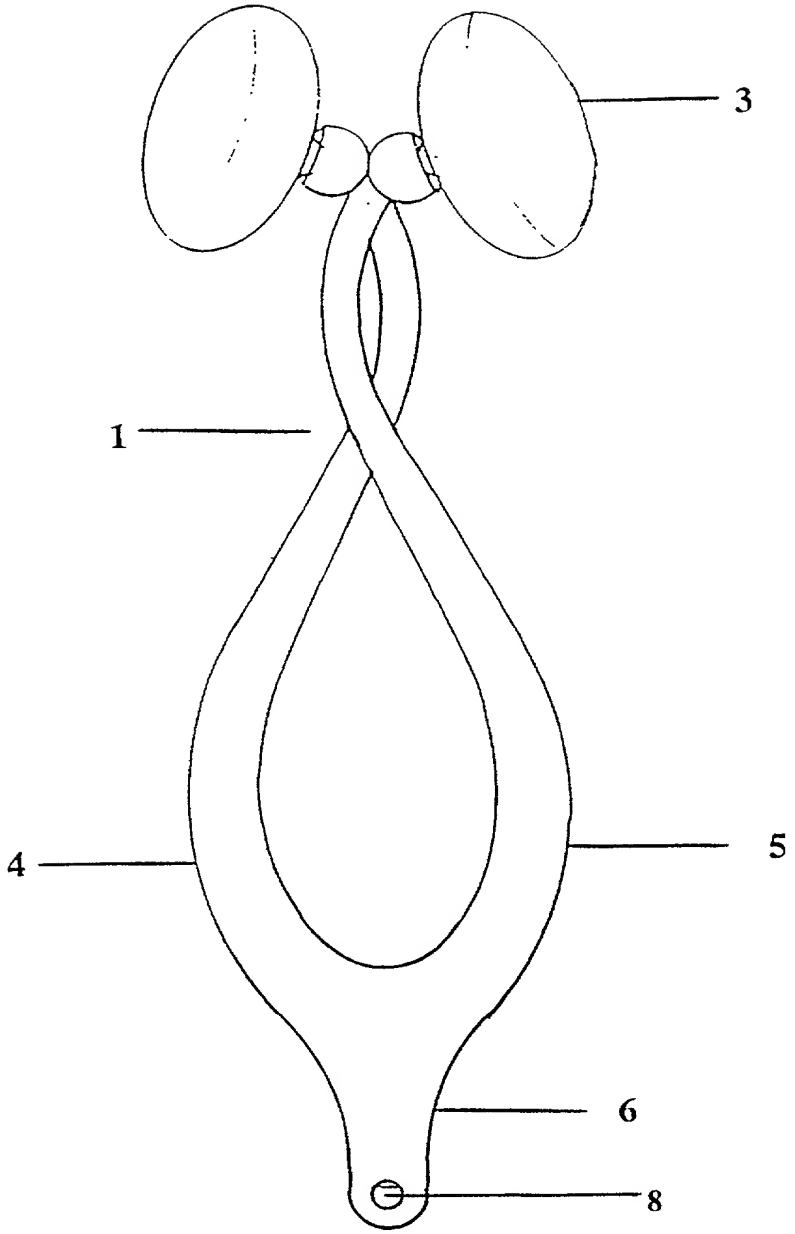


FIG 2



Attorney Docket No. _____

## DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that: my residence, post office address and citizenship are as stated below next to my name; I believe I am the original, first, and sole inventor (if only one name is listed below) or an original, first, and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled: DRUG DELIVERY SYSTEM

_____ the specification of which ☐ is attached and/or ☐ was filed on 7 April 2000 as United States Application Serial No. _____ or PCT International Application No. _____ and was amended on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above. I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR § 1.56.

I hereby claim foreign priority benefits under 35 U.S.C. § 119(a)-(d) or § 365(b) of any foreign application(s) for patent or inventor's certificate or § 365(a) of any PCT international application(s) designating at least one country other than the United States, listed below and have also identified below, any foreign application(s) for patent or inventor's certificate, or any PCT International application(s) having a filing date before that of the application(s) of which priority is claimed:

| Country | Application Number | Date of Filing | Priority Claimed Under 35 U.S.C. |
|---|---|---|---|
| New Zealand | 328967 | 10/10/97 | ☐ YES ☐ NO |
| PCT | NZ98/00147 | 6/10/98 | ☐ YES ☐ NO |

I hereby claim the benefit under 35 U.S.C. § 119(e) of any United States provisional application(s) listed below:

| Application Number | Date of Filing |
|---|---|
| | |
| | |

I hereby claim the benefit under 35 U.S.C. § 120 of any United States application(s) or § 365(c) of any PCT International application(s) designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application(s) in the manner provided by the first paragraph of 35 U.S.C. § 112, I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR § 1.56 which became available between the filing date of the prior application(s) and the national or PCT International filing date of this application:

| Application Number | Date of Filing | Status (Patented, Pending, Abandoned) |
|---|---|---|
| | | |

I hereby appoint the following attorney and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith. FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P., Douglas B. Henderson, Reg. No. 20,291; Ford F. Farabow, Jr., Reg. No. 20,630; Arthur S. Garrett, Reg. No. 20,338; Donald R. Dunner, Reg. No. 19,073; Brian G. Brunsvold, Reg. No. 22,593; Tipton D. Jennings, IV, Reg. No. 20,645; Jerry D. Voight, Reg. No. 23,020; Laurence R. Hefter, Reg. No. 20,827; Kenneth E. Payne, Reg. No. 23,098; Herbert H. Mintz, Reg. No. 26,691; C. Larry O'Rourke, Reg. No. 26,014; Albert J. Santorelli, Reg. No. 22,610; Michael C. Elmer, Reg. No. 25,857; Richard H. Smith, Reg. No. 20,609; Stephen L. Peterson, Reg. No. 26,325; John M. Romary, Reg. No. 26,331; Bruce C. Zotter, Reg. No. 27,680; Dennis P. O'Reilley, Reg. No. 27,932; Allen M. Sokal, Reg. No. 26,695; Robert D. Bajefsky, Reg. No. 25,387; Richard L. Stroup, Reg. No. 28,478; David W. Hill, Reg. No. 28,220; Thomas L. Irving, Reg. No. 28,619; Charles E. Lipsey, Reg. No. 28,165; Thomas W. Winland, Reg. No. 27,605; Basil J. Lewris, Reg. No. 28,818; Martin I. Fuchs, Reg. No. 28,508; E. Robert Yoches, Reg. No. 30,120; Barry W. Graham, Reg. No. 29,924; Susan Haberman Griffen, Reg. No. 30,907; Richard B. Racine, Reg. No. 30,415; Thomas H. Jenkins, Reg. No. 30,857; Robert E. Converse, Jr., Reg. No. 27,432; Clair X. Mullen, Jr., Reg. No. 20,348; Christopher P. Foley, Reg. No. 31,354; John C. Paul, Reg. No. 30,413; Roger D. Taylor, Reg. No. 28,992; David M. Kelly, Reg. No. 30,953; Kenneth J. Meyers, Reg. No. 25,146; Carol P. Einaudi, Reg. No. 32,220; Walter Y. Boyd, Jr., Reg. No. 31,738; Steven M. Anzalone, Reg. No. 32,095; Jean B. Fordis, Reg. No. 32,984; Barbara C. McCurdy, Reg. No. 32,120; James K. Hammond, Reg. No. 31,964; Richard V. Burgujian, Reg. No. 31,744; J. Michael Jakes, Reg. No. 32,824; Thomas W. Banks, Reg. No. 32,719; Christopher P. Isaac, Reg. No. 32,616; Bryan C. Diner, Reg. No. 32,409; M. Paul Barker, Reg. No. 32,013; Andrew Chanho Sonu, Reg. No. 33,457; David S. Forman, Reg. No. 33,694; Vincent P. Kovalick, Reg. No. 32,867; James W. Edmondson, Reg. No. 33,871; Michael R. McGurk, Reg. No. 32,045; Joann M. Neth, Reg. No. 36,363; Gerson S. Panitch, Reg. No. 33,751; Cheri M. Taylor, Reg. No. 33,216; Charles E. Van Horn, Reg. No. 40,266; Linda A. Wadler, Reg. No. 33,218; Jeffrey A. Berkowitz, Reg. No. 36,743; Michael R. Kelly, Reg. No. 33,921; James B. Monroe, Reg. No. 33,971; Doris Johnson Hines, Reg. No. 34,629; Allen R. Jensen, Reg. No. 28,224; Lori Ann Johnson, Reg. No. 34,498; and David A. Manspeizer, Reg. No. 37,540 and _____. Please address all correspondence to FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P. 1300 I Street, N.W., Washington, D.C. 20005, Telephone No. (202) 408-4000.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

| Full Name of First Inventor | Inventor's Signature | Date |
|---|---|---|
| Graham Francois Duirs | | 26.5.00 |
| Residence: 17 MacFarlane Street, Hamilton, New Zealand NZ | | Citizenship: New Zealand |
| Post Office Address: 17 MacFarlane Street, Hamilton, New Zealand | | |

Listing of Inventors Continued on Page 2 hereof. ☐ Yes ☐ No